EPINEPHrine for Anaphylaxis: Autoinjector or 1-mg Vial or Ampoule?

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Anaphylaxis is a medical emergency that requires immediate treatment with EPINEPHrine injection. The condition is becoming more common outside of the hospital due to increases in food allergies and the use of contrast media, chemotherapy, and monoclonal antibodies in outpatient clinics. Cases of anaphylaxis will likely increase along with growth of the use of monoclonal antibodies and biosimilars.

EPINEPHrine Autoinjectors

For anaphylactic reactions that occur in community settings, EPINEPHrine autoinjectors provide patients and families with greater availability and access to the drug. Those at risk should be prescribed an autoinjector and be properly trained to use it. Autoinjectors can also be found in office practices, clinics, and other locations outside of the hospital. Some hospitals also provide autoinjectors to treat anaphylaxis for inpatients, so they can sometimes be found in the emergency department or other clinical areas in unit stock or automated dispensing cabinets (ADCs) in hospitals.

An intramuscular (IM) dose of 0.3 to 0.5 mg of EPINEPHrine is recommended for anaphylaxis in adults, but no comparative trials have been conducted to determine which dose is most clinically effective. Autoinjectors of 0.3 mg are available for adult use, and repeat doses are recommended at five to 15 minute intervals until symptoms improve. Products are available in two-packs in case a second dose is needed in outpatient settings before treatment is available from emergency personnel. A 0.01-mg/kg dose is recommended for infants and children. A 0.15-mg autoinjector is available, but that dose is greater than the recommended dose for children weighing less than 15 kg.

Errors With 1-mg Ampoules or Vials

In 2014, the National Comprehensive Cancer Network (NCCN) sent a letter to member hospitals calling for deployment of EPINEPHrine autoinjectors as a way to avoid wrong-dose and wrong-route errors (e.g., intravenous [IV] instead of IM) when ampoules or vials are used for severe allergic reactions or anaphylaxis. The concern with 1-mg ampoules or vials of EPINEPHrine is that the contents must be drawn into a syringe. Unfortunately, during a stressful emergency situation, this has sometimes led to the erroneous administration of the full 1-mg dose via IV, which could prove harmful to some patients. In a review of more than 600 cases reported to the Pennsylvania Patient Safety Reporting System, wrong-route errors involving IV administration instead of IM or subcutaneous injection were responsible for 25.4% of all EPINEPHrine adverse events and 63.3% of the harmful events.[1]

Errors With Autoinjectors

There are three brands of autoinjectors available in the U.S., but they are not interchangeable with respect to training and the way they are used. Given that anaphylaxis may not occur very often at any one location, remembering how to use different devices is difficult. Patients often forget how to use them within three months,[2] and many health professionals have never been trained to use them at all.

EpiPen (Mylan) is the most commonly used device, although it has been plagued by occasional misuse when people hold it upside down, press, and inject their thumb, or when a child gains access to the device and presses the wrong end. Both situations have been reported to the Institute for Safe Medication Practices (ISMP), most recently a thumb injection by a nurse. Auvi-Q (Kaleo, Inc.) is another brand of autoinjector, which may be easier to use than the EpiPen because it provides digital voice instruc-

Are You Ready to Treat Anaphylaxis?

Can you say for sure that health care professionals in your organization are always prepared to treat an anaphylactic reaction? A 51-year-old man died after he was not properly monitored or treated for an anaphylactic reaction that occurred when he was administered an injection of iron dextran (Infed, Actavis Pharma, Inc.). While the Infed package insert states that EPINEPHrine should be immediately available in the event of an acute hypersensitivity reaction, the EPINEPHrine was not near the bedside. The patient's nurse called a rapid response team but did not believe she was permitted to obtain EPINEPHrine from a nearby crash cart before the team arrived because it would require a physician's order to administer. Requiring a specific physician's order to administer lifesaving EPINEPHrine in the event of anaphylaxis has been observed at other hospitals, as well.

Please review your policies, procedures, and/or protocols for treating anaphylaxis. When the risk of anaphylaxis is high, be sure EPINEPHrine is immediately available. Make sure that all clinicians are aware of the proper use of EPINEPHrine kits or autoinjectors. Be explicit in a medical staff-approved protocol about the conditions under which qualified professionals, including nurses, may administer a lifesaving EPINEPHrine dose. In the absence of a protocol or order, as in the case above, a qualified clinician might still administer a dose of EPINEPHrine using an available single-dose autoinjector, considering administration without an order is the lesser of two evils if the patient's life is hanging in the balance. Health care leaders should not put staff in a position where such a decision might be necessary—be sure you are ready for anaphylaxis!

tions, and the needle retracts to lessen the risk of a needle-stick injury. A generic autoinjector from Lineage Pharmaceuticals, which costs about 20% less than the other brands, is more difficult to use. The product won't be familiar to those who currently know how to use one of the other autoinjectors. Also, ISMP recently informed Lineage Pharmaceuticals that its pen lacks a barcode, which the company promised to address.

Needle Length and Cost of EPINEPHrine Autoinjectors

There are other drawbacks that have blocked full implementation of autoinjectors in clinical areas. For one, although giving EPINEPHrine by the IM route is most effective, there is no consensus about available autoinjector needle length. People worry that the relatively short needle length (16.5 mm) on pens might not ensure that the drug reaches into the muscle when injected into the lateral thigh, especially in women.[3] On the other hand, autoinjectors have proved effective in treating anaphylaxis, and there is at least some evidence that the pressure exerted during the forceful injection is adequate enough to drive EPINEPHrine past the depth of the needle into the muscle.[4,5]

Although we believe that safety trumps cost, it's hard not to notice that the cost of an autoinjector has increased for a two-pack. This is unfortunate because it may impact a patient's access to autoinjectors. Fortunately, insurance generally covers the cost of autoinjectors for consumers, but there is an associated copay.[6]

For health systems that use these and store them in numerous locations throughout their organization, hundreds of thousands of dollars may be needed annually to stock these devices, which can significantly affect the budget. In addition, staff training and inventory needs have to be considerable when determining the cost. EPINEPHrine autoinjectors have a shelf life of only 12–18 months. Thus, they may not be used prior to expiration, resulting in wasted inventory and increases in cost. Special attention is also needed for organizations that may stock the autoinjectors in ADCs. The expiration date should be closely monitored and stock rotated on a regular basis. Our attention was drawn recently to an emergency medical service in Kings County, Washington, that did away with autoinjectors due to the high cost, replacing them with an anaphylaxis kit. They reasoned that an ampoule or vial of EPINEPHrine 1 mg would cost about $1.25. Add in a syringe, alcohol wipe, needle, and so on, and the savings are still significant. Some hospitals have taken the same course of action.

Autoinjector or 1-mg Vial or Ampoule?

Deciding between the autoinjector or 1-mg vial or ampoule remains a tough choice. Some hospitals have decided that autoinjector manufacturers have priced themselves out of the market, making it difficult to allow use in all areas of the hospital. Instead, they have decided to stock 1-mg ampoules or vials, or for safety, they have prepared kits containing a 1-mg EPINEPHrine ampoule or vial along with a syringe, needle, label with proper dose for IM injection, a warning not to administer the entire vial, and any other essential components. Still, we agree with NCCN that the presence of a vial or ampoule of EPINEPHrine in the wrong hands invites accidental IV injection when the patient has an IV line established. So, an EPINEPHrine autoinjector is appealing as a properly labeled unit dose that can be employed within seconds to treat the emergency, and the contents cannot be administered via IV.

To ISMP, an autoinjector certainly makes sense in outpatient clinics and office practices. Examples include outpatient areas where chemotherapy or contrast media is administered. If more than one ADC is available, the autoinjectors should be stocked in only one of them with visual aids available on the others to guide staff to the correct ADC when it is needed. If you choose to use an autoinjector, ISMP favors the Auvi-Q device because it provides digital voice instructions to "talk" users through the injection process and is easy to use, even for those not completely familiar with it. However, staff training as well as periodic retraining about proper use of the autoinjector is still a requirement.

REFERENCES

1. Pennsylvania Patient Safety Authority. An update in the "Epi"demic: events involving EPINEPHrine. *Pa Patient Safe Advis* 2009;6(3):102–103.
2. Lowry F. Patients forget how to use EpiPen after 3 months. November 20, 2012. Medscape Medical News. Available at: www.medscape.com/viewarticle/774843. Accessed October 23, 2017.
3. Bhalla MC, Gable BD, Frey JA, et al. Predictors of epinephrine autoinjector needle length inadequacy. *Am J Emerg Med* 2013;31(12):1671–1676.
4. Baker TW, Webber CM, Stolfi A, Gonzalez-Reyes E. The TEN study: time epinephrine needs to reach muscle. *Ann Allergy Asthma Immunol* 2011;107(3):235–238.
5. Lieberman P. The 10-second rule and other myths about epinephrine and auto-injectors. *Ann Allergy Asthma Immunol* 2011;107(3):189–190.
6. Kids with Food Allergies Foundation Community. What to do if you can't afford epinephrine auto-injectors. January 22, 2015. Available at: https://community.kidswithfoodallergies.org/blog/what-to-do-if-you-cant-afford-epinephrine-auto-injectors. Accessed October 23, 2017.

The reports described in this column were received through the ISMP Medication Errors Reporting Program (MERP). Errors, close calls, or hazardous conditions may be reported on the ISMP website (www.ismp.org) or communicated directly to ISMP by calling 1-800-FAIL-SAFE or via email at ismpinfo@ismp.org. ■

ISMP Launches First High-Alert Medication Safety Self-Assessment

The Institute for Safe Medication Practices (ISMP) has introduced a new tool to help hospitals, long-term-care facilities, and certain outpatient facilities evaluate their best practices related to high-alert medications, identify opportunities for improvement, and track their experiences over time. The *ISMP Medication Safety Self Assessment® for High-Alert Medications* focuses on general high-alert medications and 11 specific medication categories—including opioids, insulin, neuromuscular blocking agents, chemotherapy, and moderate and minimal sedation. Participants who submit assessment findings to ISMP anonymously via a secure Internet portal by **February 28, 2018**, will be able to obtain their weighted scores so they can compare themselves to demographically similar organizations. Participation can also help organizations meet requirements for managing high-alert medications from regulatory and accrediting agencies, such as the Centers for Medicare and Medicaid Services and The Joint Commission. To access the self-assessment workbook, visit: www.ismp.org/selfassessments/SAHAM.